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# Stereoselective Isomerization Reaction of (Iminodiacetato)(ethylenediamine-*N*-acetato)cobalt(III), [Co(ida)(edma)], in a Basic Aqueous Solution

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Isomerization reactions among four geometrical isomers (pink, violet, brown, and light-brown) of [Co(ida)(edma)] were studied in a basic aqueous solution. In a reaction of $(-)^{\rm CD}_{554}$-pink, three isomers of $(+)^{\rm CD}_{563}$-violet, $(+)^{\rm CD}_{565}$-brown (with a low optical purity), and racemic light-brown formed simultaneously. The major products in reactions of $(+)^{\rm CD}_{563}$-violet and $(+)^{\rm CD}_{565}$-brown were $(+)^{\rm CD}_{565}$-brown and $(+)^{\rm CD}_{563}$-violet, respectively. Light-brown mainly isomerized to brown at a rapid rate. Moreover, it was found that $(+)^{\rm CD}_{563}$-violet racemized at a considerable rate. These stereoselective reactions are discussed in connection with those for $[{\rm Co(edma)_2}]^+$ and $[{\rm Co(ida)_2}]^-$.

Over the last few years we have been investigating the structure-reactivity pattern of octahedral complexes, particularly the isomerization of the bis(terdentate)cobalt(III) complexes. In previous papers,[1,2] we reported the preparation and characterization of four geometrical isomers of [Co(ida)(edma)] (Fig. 1),[3] and also a determination of the absolute configurations of the three isomers containing facially coordinated ligands. The possible configurations and CD signs for the three isomers are shown in Table 1. We describe here the isomerization reaction of the [Co(ida)(edma)] system, which is discussed on the basis of the previous studies on the related complexes, $[{\rm Co(ida)_2}]^-$[4] and $[{\rm Co(edma)_2}]^+$.[5]

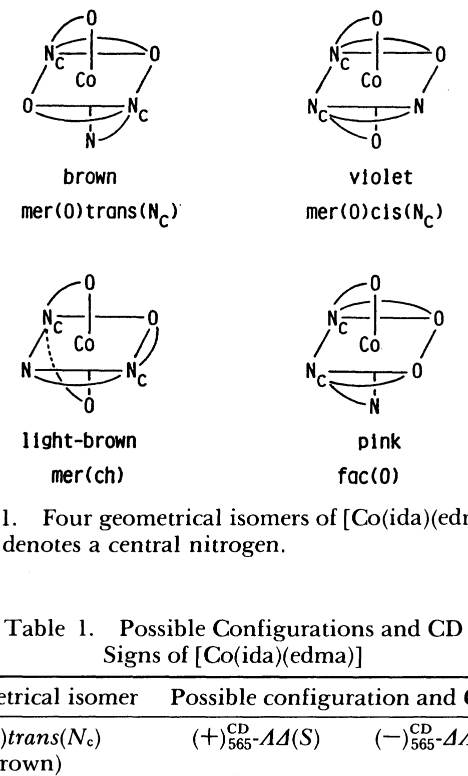


Fig. 1. Four geometrical isomers of [Co(ida)(edma)]. $N_c$ denotes a central nitrogen.

Table 1. Possible Configurations and CD Signs of [Co(ida)(edma)]

| Geometrical isomer | Possible configuration and CD sign | |
|---|---|---|
| *mer(O)trans*($N_c$)<br>(brown) | $(+)^{\rm CD}_{565}$-$\Delta\Delta(S)$ | $(-)^{\rm CD}_{565}$-$\Lambda\Lambda(R)$ |
| *mer(O)cis*($N_c$)<br>(violet) | $(+)^{\rm CD}_{563}$-$\Lambda\Delta\Delta(S)$ | $(-)^{\rm CD}_{563}$-$\Delta\Lambda\Lambda(R)$ |
| *fac(O)*<br>(pink) | $(+)^{\rm CD}_{554}$-$\Lambda\Delta\Delta(S)$ | $(-)^{\rm CD}_{554}$-$\Delta\Lambda\Lambda(R)$ |

## Experimental

**Complexes and Reagents.** The complexes examined here were prepared and optically resolved according to methods described in our previous papers.[1,2] They are $(+)^{\rm CD}_{565}$-*mer(O)trans*($N_c$)-[Co(ida)(edma)] (abbreviation: $(+)^{\rm CD}_{565}$-brown), $(+)^{\rm CD}_{563}$-*mer(O)cis*($N_c$)-[Co(ida)(edma)]·$H_2O$ ($(+)^{\rm CD}_{563}$-violet), $(-)^{\rm CD}_{554}$-*fac(O)*-[Co(ida)(edma)] ($(-)^{\rm CD}_{554}$-pink), and *mer(ch)*-[Co(ida)(edma)]·$H_2O$ (light-brown). All the chemicals used were of a reagent grade, and the deionized water was degassed before use.

**Isomerization. $(+)^{\rm CD}_{563}$-Violet Isomer:** This isomer (0.2211 g) was dissolved in 100.0 cm$^3$ of water in a reaction vessel kept in a thermostated bath at 40.0 °C. The reaction was started by stirring 100.0 cm$^3$ of a buffer solution [$Na_2CO_3$(0.5606 g)-$NaHCO_3$(0.2241 g)] previously kept at 40.0 °C into the reaction vessel. The reaction conditions were as follows: Complex concentration, $3.4\times10^{-3}$ M (M= mol dm$^{-3}$); pH, 10.30±0.03; temperature, 40.0±0.1 °C. The temperature and pH of the reaction solution were checked with a thermistor thermometer (Takara D221) and a pH meter (Toa TSC-10A), respectively, throughout the kinetic run. At a prescribed time, the reaction solution was acidified to pH 5 in order to stop the reaction. (Such kinetic runs with different reaction times were carried out repeatedly.) The acidified solution was concentrated under reduced pressure at 35—40 °C and then applied to a column (3.0 cm×80 cm) of Sephadex G-10 in order to remove salts.[6] The eluate containing the isomers of [Co(ida)(edma)] was concentrated again and chromatographed on a column (3.7 cm×80 cm) of QAE-Sephadex A-25 [$\rm Sb_2(\textit{d}\text{-tart})_2^{2-}$ form] using water as an eluent; three bands of el 1 [$(+)^{\rm CD}_{565}$-brown and violet], el 2 [$(-)^{\rm CD}_{565}$-brown and light brown], and el 3 [pink]. The three eluates were collected separately and concentrated to appropriate constant volumes. The amount and optical purity of each isomer were determined from absorption and CD data measured by a Hitachi 557 spectrophotometer and a JASCO J-22 spectropolarimeter, respectively. The amounts of the two isomers and the optical purity of violet in el 1 were estimated from binary-curve analyses of the absorption and CD spectra. The amounts of the two isomers in el 2 were also estimated by a procedure similar to that described above.

In these curve analyses, the spectral data at 20 points in the visible region were used; the analyses were carried out on an NEC PC-9801F computer using a least-squares method.

**$(+)^{\rm CD}_{565}$-Brown, $(-)^{\rm CD}_{554}$-Pink, and Light-Brown Isomers:** The isomerization reaction of $(+)^{\rm CD}_{565}$-brown was carried out by a procedure similar to that used for $(+)^{\rm CD}_{563}$-violet. The reaction conditions were the same as those in the case of $(+)^{\rm CD}_{563}$-violet.

The solubility of $(-)^{\rm CD}_{554}$-pink was low. Thus, the saturated solution (180 cm$^3$) of $(-)^{\rm CD}_{554}$-pink, which was obtained by stirring the powder of the isomer in water at 40.0 °C for 10 min, and a buffer solution (20 cm$^3$) containing 0.5653 g of $Na_2CO_3$ and 0.2241 g of $NaHCO_3$ were prepared for the isomerization reaction. The procedure of the reaction was the same as that in the case of $(+)^{\rm CD}_{563}$-violet. The reaction conditions were as follows: Complex concentration, $2.8 \times 10^{-3}$ M (It was determined from the absorption data at the start of the reaction.); pH, $10.30 \pm 0.02$; temperature, $40.0 \pm 0.1$ °C.

The isomerization study of light-brown could not be carried out sufficiently, since the preparation of the isomer was very difficult. Only one isomerization run using light-brown as a starting material was carried out on a small scale (1/4 of the scale for violet), and the isomer proportions at one hour after the start of the reaction were determined by a procedure similar to that in the case of $(+)^{\rm CD}_{563}$-violet.

In weak acidic and neutral solutions at room temperature, the absorption and CD spectral changes of each isomer were not observed for about one day. Therefore, progress of the isomerization and/or racemization reaction during such procedures as chromatographic separation and concentration under reduced pressure should be negligible.

## Results and Discussion

**Base-Catalyzed Isomerization Reaction. $(-)^{\rm CD}_{554}$-Pink Isomer:** The isomerization reaction of $(-)^{\rm CD}_{554}$-pink was followed over a period of 12 h under the conditions of pH 10.30 and 40.0 °C. Figure 2 shows the changes in the proportions of the starting material and reaction products. A part of the numerical data are listed in Table 2, together with the enantiomer excess percentage of each isomer. The isomerization reaction of pink is faster than the reactions of violet and brown. The half-life period (with regard to the decrease in pink) is about 40 min under the conditions described above. In this reaction, three products — $(+)^{\rm CD}_{563}$-violet, $(+)^{\rm CD}_{565}$-brown, and racemic light-brown — were simultaneously formed. Throughout the reaction, no other products were detected by the present experimental method. The brown isomer increased in amount with the passage of time and was a major species after a prolonged reaction time. The concentrations of light-brown and violet were maximal at about 45 min and about 4 h after the reaction start, respectively; thereafter, they decreased. At longer reaction times (>ca. 4 h), the amount of light-brown was almost negligible.

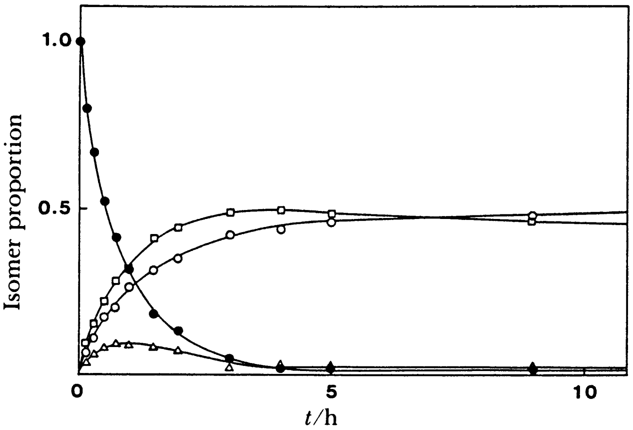


Fig. 2. The changes of the isomer proportions in the isomerization reaction of $(-)^{\rm CD}_{554}$-pink (40.0 °C, pH 10.30); pink (-●—●-), violet(-□—□-), brown (-○—○-), and light-brown (-△—△-).

As shown in Table 2, $(-)^{\rm CD}_{554}$-pink (starting material) retained a high optical purity until about 2 h; at that time most of the pink had already isomerized to other isomers. This fact probably indicates that the racemization of $(-)^{\rm CD}_{554}$-pink, itself, is negligible. During the initial stage of the reaction, $(+)^{\rm CD}_{563}$-violet formed from $(-)^{\rm CD}_{554}$-pink retained an optical purity of about 100%. The isomerization path of $(-)^{\rm CD}_{554}$-pink → $(+)^{\rm CD}_{563}$-violet

Table 2. The Proportions and Optical Purities of the Starting Materials and Products in the Isomerization Rreaction (40.0 °C, pH 10.30)

(i) $(-)^{\rm CD}_{554}$-pink

| t | Isomer proportion (optical purity/%) | | | |
|---|---|---|---|---|
| min | $(-)^{\rm CD}_{554}$-pink | $(+)^{\rm CD}_{565}$-brown | $(+)^{\rm CD}_{563}$-violet | light-brown |
| 10 | 0.800(100) | 0.060(14) | 0.095(100) | 0.045 |
| 30 | 0.561(100) | 0.156(9) | 0.205(100) | 0.078 |
| 60 | 0.336(100) | 0.250(10) | 0.322(87) | 0.092 |
| 120 | 0.133(92) | 0.351(10) | 0.446(61) | 0.072 |
| 240 | 0.031(50) | 0.434(12) | 0.498(49) | 0.037 |

(ii) $(+)^{\rm CD}_{563}$-violet

| t | Isomer proportion (optical purity/%) | | | |
|---|---|---|---|---|
| h | $(+)^{\rm CD}_{563}$-violet | $(+)^{\rm CD}_{565}$-brown | $(-)^{\rm CD}_{554}$-pink | light-brown |
| 1 | 0.935(92) | 0.019(71) | 0.020(100) | 0.026 |
| 3 | 0.853(53) | 0.078(50) | 0.029(65) | 0.039 |
| 5 | 0.803(46) | 0.131(28) | 0.026(53) | 0.039 |
| 8 | 0.697(21) | 0.242(24) | 0.026(25) | 0.035 |
| 13 | 0.617(8) | 0.326(14) | 0.024(13) | 0.033 |
| 24 | 0.456(0) | 0.496(8) | 0.021(3) | 0.027 |

(iii) $(+)^{\rm CD}_{565}$-brown

| t | Isomer proportion (optical purity/%) | | | |
|---|---|---|---|---|
| h | $(+)^{\rm CD}_{565}$-brown | $(+)^{\rm CD}_{563}$-violet | $(-)^{\rm CD}_{554}$-pink | light-brown |
| 2 | 0.967(98) | 0.014(70) | 0.007(25) | 0.038 |
| 5 | 0.921(94) | 0.053(22) | 0.010(17) | 0.016 |
| 8 | 0.887(89) | 0.083(16) | 0.011(15) | 0.019 |
| 13 | 0.848(83) | 0.122(9) | 0.013(14) | 0.017 |
| 30 | 0.790(79) | 0.181(0) | 0.015(0) | 0.014 |

(iv) light-brown[a]

| t | Isomer proportion | | | |
|---|---|---|---|---|
| h | light-brown | brown | violet | pink |
| 1 | 0.167 | 0.685 | 0.118 | 0.030 |

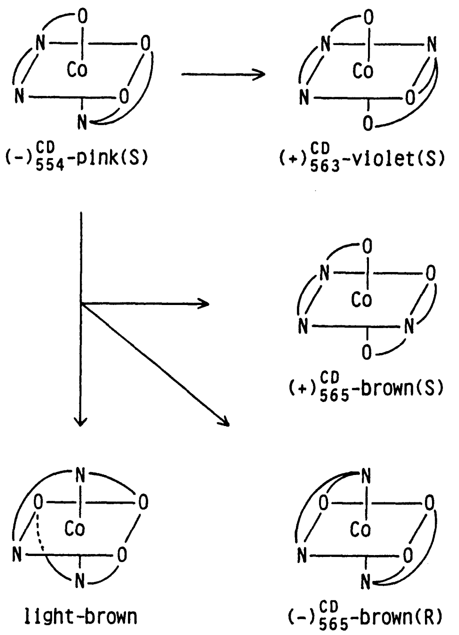
a) Reaction conditions; pH 10.28 and 40.0 °C.

change is thus highly stereoselective. However, the optical purity of the formed $(+)^{\rm CD}_{563}$-violet decreased with the passage of time. The $(+)^{\rm CD}_{565}$-brown formed in the same reaction showed a low optical purity (ca. 10 %). Moreover, the value of the optical purity was nearly constant throughout the present reaction (12 h). Accordingly, it is thought that $(-)^{\rm CD}_{554}$-pink isomerizes to $(+)^{\rm CD}_{565}$- and $(-)^{\rm CD}_{565}$-brown with a constant ratio (55 : 45%).

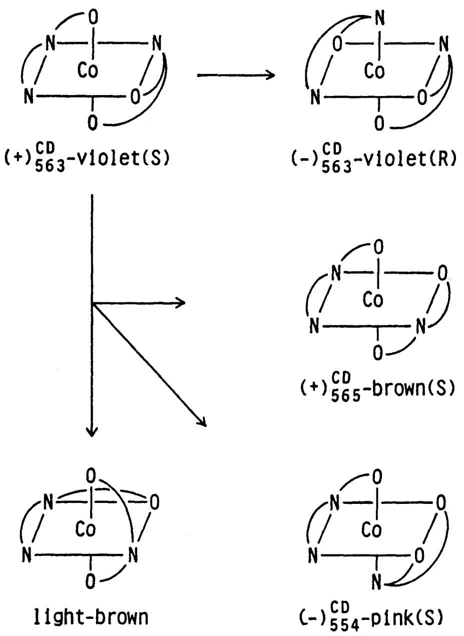
In an isomerization reaction among three geometrical isomers of $[{\rm Co(ida)_2}]^-$, the reaction scheme was found to be *u-fac* ⇄ *mer* ⇄ *s-fac*.[4] However, in the $[{\rm Co(edma)_2}]^+$ system, the isomerization from the *fac*-type isomers to the *mer* isomer was not observed. Isomerization among *fac*-type isomers of $[{\rm Co(edma)_2}]^+$ accompanies inversion at one of two secondary nitrogen (sec-N) centers of the coordinated edma ligands. The inversion is thought to be caused by a coordination-site exchange between the sec-N and carboxylato oxygen of a coordinated edma ligand.[5] If [Co(ida)(edma)] has a reactivity that is similar to those of both $[{\rm Co(ida)_2}]^-$ and $[{\rm Co(edma)_2}]^+$, the reaction paths shown in Scheme 1 should be expected for the isomerization of $(-)^{\rm CD}_{554}$-pink: Three paths from $(-)^{\rm CD}_{554}$-pink to $(+)^{\rm CD}_{563}$-violet, $(+)^{\rm CD}_{565}$-brown, and $(-)^{\rm CD}_{565}$-brown are proposed by considering the isomerization mechanism for the $[{\rm Co(edma)_2}]^+$ system (coordination-site exchange between the sec-N and O of the coordinated ida or edma ligand), and the $(-)^{\rm CD}_{554}$-pink → light-brown path is proposed on the basis of the assumption that the reaction proceeds by a process similar to that for the $[{\rm Co(ida)_2}]^-$ system. The experimental results described above, namely the simultaneous formation of $(+)^{\rm CD}_{563}$-violet, approximately racemic brown, and light-brown are well explained with the simultaneous occurence of four paths in Scheme 1. The light-brown obtained in this isomerization reaction was racemate. This does not mean that the $(-)^{\rm CD}_{554}$-pink → light-brown change is not stereoselective. Even though the change is stereoselective, the optically active light-brown formed from $(-)^{\rm CD}_{554}$-pink must racemize very rapidly under the present reaction conditions, judging from the racemization rates of *mer*-$[{\rm Co(ida)(dien)}]^+$,[7] *mer*-$[{\rm Co(edma)(dien)}]^{2+}$,[8] and *mer*-$[{\rm Co(dien)_2}]^{3+}$.[9] The decrease of the optical purities in $(+)^{\rm CD}_{563}$-violet and $(-)^{\rm CD}_{554}$-pink with the passage of time are explained in the later section.

**$(+)^{\rm CD}_{563}$-Violet Isomer:** The isomerization reaction using $(+)^{\rm CD}_{563}$-violet as a starting material was also carried out in a carbonate buffer (pH 10.30) at 40 °C, and a part of the data are listed in Table 2. In the initial stage of the reaction, three products — $(+)^{\rm CD}_{565}$-brown, $(-)^{\rm CD}_{554}$-pink, and light-brown (racemate) — were formed. The amounts of pink and light-brown little increased even though the reaction was allowed to proceed for a long time, indicating that the subsequent isomerizations from these isomers to brown and/or violet occurred. While, brown increased in its amount with the passage of time and was a major species in the final stage of the reaction.

As shown in Table 2, the optical purity of the starting material — $(+)^{\rm CD}_{563}$-violet — decreased more rapidly compared with the rate of its concentration decrease. This fact means that $(+)^{\rm CD}_{563}$-violet, itself, racemized at a considerable rate. $(-)^{\rm CD}_{554}$-Pink and $(+)^{\rm CD}_{565}$-brown, which were formed from $(+)^{\rm CD}_{563}$-violet, showed optical purities of about 100 and about 70%, respectively, during the initial stage of the reaction. These two isomerization paths are, thus, stereoselective. However, the optical purities of these two products decreased with the passage of time. The results may be attributed to a rapid



Scheme 1.



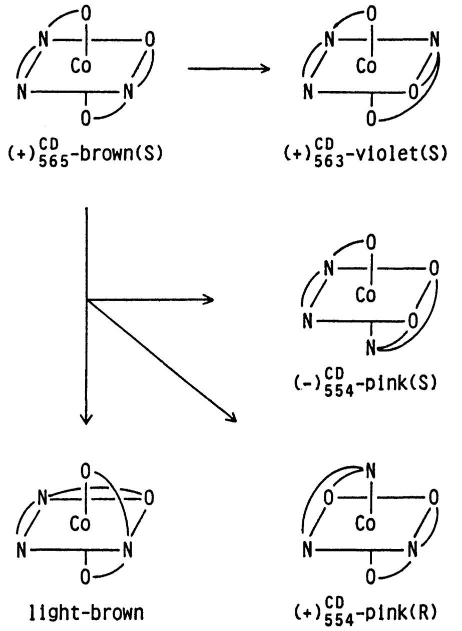
Scheme 2.

racemization of the starting material; $(-)^{CD}_{563}$-violet formed in the racemization of the starting material [$(+)^{CD}_{563}$-violet] produces $(+)^{CD}_{554}$-pink and $(-)^{CD}_{565}$-brown.

The isomerization of $(+)^{CD}_{563}$-violet can also be explained in a manner similar to that in the isomerization of $(-)^{CD}_{554}$-pink. If the isomerization due to the mechanism proposed for the $[Co(edma)_2]^+$ system occurs in $(+)^{CD}_{563}$-violet, three isomers — $(-)^{CD}_{563}$-violet, $(+)^{CD}_{565}$-brown and $(-)^{CD}_{554}$-pink — must be formed, as shown in Scheme 2. This proposal is consistent with the experimental results except for the minor formation of $(-)^{CD}_{554}$-pink. In the $[Co(edma)_2]^+$ system, it is found that the inversion at the sec-N center trans to the ligating nitrogen [*trans*(*N*)-sec-N] occurs slowly and that the inversion at the *trans*(*O*)-sec-N center occurs rapidly.5) If such phenomenon as observed in the $[Co(edma)_2]^+$ system is expected to occur in the reaction of $(+)^{CD}_{563}$-violet, the experimental results, namely, the fast racemization of $(+)^{CD}_{563}$-violet and the minor formation of $(-)^{CD}_{554}$-pink, can be rationalized: The $(+)^{CD}_{563}$-violet → $(-)^{CD}_{563}$-violet change (racemization) accompanies the inversion at *trans*(*O*)-sec-N center, therefore, its rate is fast, and the $(+)^{CD}_{563}$-violet → $(-)^{CD}_{554}$-pink change accompanying the inversion at *trans*(*N*)-sec-N center occurs slowly. The formation rate of brown from $(+)^{CD}_{563}$-violet is relatively faster than that of pink in the same reaction, even though the $(+)^{CD}_{563}$-violet → $(+)^{CD}_{565}$-brown change accompanies an inversion at *trans*(*N*)-sec-N center. This fact may be ascribed to additional isomerization paths, such as $(+)^{CD}_{563}$-violet → $(-)^{CD}_{554}$-pink → $(+)^{CD}_{565}$-brown and $(+)^{CD}_{563}$-violet → light-brown → brown.

$(+)^{CD}_{563}$-Violet isomerized to racemic light-brown in a small amount. This indicates the existence of isomerization due to a mechanism similar to that in the $[Co(ida)_2]^-$ system, even though it is a minor path in the isomerization of $(+)^{CD}_{563}$-violet.

**$(+)^{CD}_{565}$-Brown Isomer:** The isomerization reaction of $(+)^{CD}_{565}$-brown proceeded slowly. The major product was $(+)^{CD}_{563}$-violet, of which the optical purity was high during the initial stage of the reaction (Table 2). $(-)^{CD}_{554}$-Pink with low optical purity and light-brown were also formed in a small amount; their amounts did not increase with time. This result can be rationalized using the same idea as used for the isomerization of $(+)^{CD}_{563}$-violet. If the isomerization of $(+)^{CD}_{565}$-brown proceeds on the mechanism of the coordination-site exchange between the sec-N and O of the edma or ida ligand, three products of $(+)^{CD}_{563}$-violet and $(-)^{CD}_{554}$- and $(+)^{CD}_{554}$-pink may be formed (Scheme 3). Two sec-N atoms in brown are located at the trans positions to each other [*trans*(*N*)-sec-N]; therefore, the isomerization of brown is expected to be slow. This expectation coincides with the present experimental result. The formation of light-brown can be explained by assuming an isomerization path similar to that proposed for the $[Co(ida)_2]^-$ system, even though it is a minor path in this reaction.



Scheme 3.

**Light-Brown Isomer:** The isomerization study of light-brown was not sufficient, since the preparation of its isomer was very difficult. The absorption spectrum of light-brown changed more rapidly, compared with the spectral changes of other isomers. From this spectral change, the formations of brown (major) and violet (minor) were presumed. Light-brown was allowed to react for one hour under the conditions of pH 10.28 at 40.0 °C; the proportions of the starting material and products in the reaction solution were chromatographically obtained. As shown in Table 2, the major product was brown (83% of the total amount of the products) one hour after the reaction started.

In the previous section it was described that $(+)^{CD}_{565}$-brown with a very low optical purity was obtained in the isomerization reaction of $(-)^{CD}_{554}$-pink. The result has been explained by the occurrence of two different N–O displacement processes (Scheme 1). The formation of racemic brown from $(-)^{CD}_{554}$-pink was also expected through the successive path of $(-)^{CD}_{554}$-pink → light-brown → brown (with a rapid rate). This path is similar to the isomerization process in the $[Co(ida)_2]^-$ system. It may be sure that the pink → light-brown → brown change contributes to the isomerization of pink to a considerable extent.

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3) Abbreviations used: ida, iminodiacetate dianion; edma, ethylenediamine-*N*-acetate monoanion; dien, 3-azapentane-1,5-diamine.

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